Remarks

Claims 23-29 are pending and amended to define a dosage formulation . Support for the amendment is found in the specification at page 10, lines 16-19

The present invention is directed to dosage formulations that lower cholesterol in an amount effective to decrease production of amyloid β (Aβ) protein in neuronal cells.

Rejection Under 35 U.S.C. § 102

Claims 23-29 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,866,090 to Hoffman *et al.* ("Hoffman"); U.S. Patent No. 5,350,758 to Wannamaker *et al.* ("Wannamaker"); and U.S. Patent No. 5,362,732 to Spielvogel *et al.* ("Spielvogel"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Spielvogel discloses a class of boronated compounds that reduce serum cholesterol levels upon administration to mice (Example 15). Hoffman discloses analogs of lovastatin and related analogs which are useful alone or in combination with bile acid sequestrants as antihypercholesterolemic agents (column 9, lines 50-53, lines 63-66). Wannamaker discloses piperidyl sulfonamides and sulfoxamides which are inhibitors of cholesterol biosynthesis and are useful in lowering serum cholesterol levels (column 2, lines 12-17).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). A 102 rejection over multiple references is proper when the extra references cited show that a characteristic not

disclosed is inherent. To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

The claims have been amended to define dosage formulations providing an effective amount of a cholesterol-lowering compound which is able to cross the blood brain barrier to decrease production of Aβ in neuronal cells. The pharmacological effects cited in the prior art are not described as being present in an amount that decreases production of Aβ protein in neuronal cells nor is there any indication that the compounds disclosed are able to cross the blood brain barrier or have any effect on production of Aβ protein in neuronal cells.

Moreover, **the dosages that are effective in lowering cholesterol versus lowering the amount of amyloid precursor protein are different.** The Examiner is respectfully directed to page 3, lines 11-13, which indicates that a 10% decrease in serum cholesterol levels is believed to be sufficient to decrease production of Aβ protein in neurons. Such a decrease would not be clinically effective in treating hypercholesterolemia (see Spielvogel, Example 15).

Rejection Under 35 U.S.C. § 103

Claims 26 and 27 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,350,758 to Wannamaker *et al.* Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

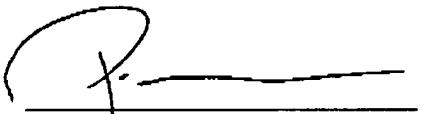
Wannamaker discloses pharmaceutical compositions which inhibit 2,3-oxidosqualene cyclase and as a result inhibit cholesterol biosynthesis. Example 10 describes the purification of oxidosqualene cyclase from rat liver. The compounds disclosed by Wannamaker are tested to determine their ability to inhibit the conversion of Squalene monoepoxide to lanosterol catalyzed by purified oxidosqualene cyclase. This suggests that the disclosed compounds inhibit biosynthesis of cholesterol in the liver. There is no indication that these compounds are able to cross the blood brain barrier or would have any effect on the production of Aβ protein in

neuronal cells. One of ordinary skill in the art would not be motivated to use the compounds disclosed by Wannamaker to inhibit the production of Aβ protein in neuronal cells.

Accordingly, the dosages required to decrease production of Aβ protein is different and to the extent it is relevant the patient population may be different. The prior art does not suggest that lowering cholesterol would have any effect on the treatment of Alzheimer's disease. Therefore, the claimed subject matter is novel.

Allowance of claims 23-29 is respectfully solicited.

Respectfully submitted,



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